UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,430	04/08/2004	Charli Kruse	B1180/20026	7174

3000 7590 04/29/2008

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.
11TH FLOOR, SEVEN PENN CENTER
1635 MARKET STREET
PHILADELPHIA, PA 19103-2212

EXAMINER	
HAMA, JOANNE	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
04/29/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@crbcp.com

Office Action Summary	Application No.	Applicant(s)	
	10/820,430	KRUSE, CHARLI	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,5-14 and 48-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,5-14 and 48-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 24, 2008 has been entered.

Claims 1, 2, 4, 15-47 are cancelled. Claims 3, 5-10, 14 are amended. Claims 48-51 are new. With regard to the species election of site where acinar tissue is obtained, Applicant elected, without traverse, pancreas, as the site (Applicant's response, September 25, 2006.

Claims 3, 5-14, 48-61 are under consideration.

New/Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 5-14 remain rejected in modified form and claims 48-61 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Upon further consideration, a new issue of enablement is addressed as follows. Response to Applicant's rebuttals, filed January 24, 2008, follows the new issue of enablement.

The total lack of enablement is raised based on the lack of evidence in the specification that the claimed cells express surface antigens that characterize pluripotent cells and that the claimed cells have a normal karyotype. The NIH lists its criteria for ES cells (see NIH, Stem Cell Information, Stem Cell Basics, IIIC, <http://stemcells.nih.gov/info/basics/basics3.asp>).

- growing and subculturing the stem cells for many months. This ensures that the cells are capable of long-term self-renewal. Scientists inspect the cultures through a microscope to see that the cells look healthy and remain undifferentiated.
- using specific techniques to determine the presence of surface markers that are found only on undifferentiated cells. Another important test is for the presence of a protein called Oct-4, which undifferentiated cells typically make. Oct-4 is a transcription factor, meaning that it helps turn genes on and off at the right time, which is an important part of the processes of cell differentiation and embryonic development.
- examining the chromosomes under a microscope. This is a method to assess whether the chromosomes are damaged or if the number of chromosomes has changed. It does not detect genetic mutations in the cells.
- determining whether the cells can be subcultured after freezing, thawing, and replating.
- testing whether the human embryonic stem cells are pluripotent by 1) allowing the cells to differentiate spontaneously in cell culture; 2) manipulating the cells so they will differentiate to form specific cell types; or 3) injecting the cells into an immunosuppressed mouse to test for the formation of a benign tumor called a teratoma. Teratomas typically contain a mixture of many differentiated or partly differentiated cell types—an indication that the embryonic stem cells are capable of differentiating into multiple cell types.

While the instant specification teaches that the pancreatic stem cells can differentiate into nerve cells (expressing PGP 9.5. and NF), glial cells (expressing S100 and GFAP), muscle cells (expressing SMA), cartilage (expressing collagen type II), exocrine glandular cells (expressing amylase and trypsin), endocrine glandular cells (expressing insulin) and epidermal cells (expressing cytokeratin), following organoid body formation, the specification does not teach that the instant cells express cell surface markers associated with pluripotent cells and that they exhibit a normal karyotype.

Applicant's arguments filed January 24, 2008 have been fully considered and but they are not persuasive.

With regard to the breadth of the claims encompassing pluripotent cells obtained from pancreas of any species of mammal, Applicant provides a 132 declaration, filed February 26, 2008, indicating that pluripotent stem cells were obtained from the salivary glands of goats (Applicant's response, page 5). The 132 of February 26, 2008 does not provide support to enable the full scope of pluripotent stem cells obtained from pancreas of any mammal. While the specification provides guidance for pluipotent stem cells from rat and human pancreas, wherein the cells differentiate into nerve cells (expressing PGP 9.5. and NF), glial cells (expressing S100 and GFAP), muscle cells (expressing SMA), cartilage (expressing collagen type II), exocrine glandular cells (expressing amylase and trypsin), endocrine glandular cells (expressing insulin) and epidermal cells (expressing cytokeratin), following organoid body formation, the 132 does not teach that pancreatic tissue from goat differentiates into the same cell types as

that of rat and human. As indicated in the Office Action, December 15, 2006, pages 5-6, Pera et al. teach that pluripotent stem cells between different species of animals do not behave the same way. As such, the specification and art at the time of filing do not provide guidance for an artisan to arrive at pluripotent stem cells obtained from the pancreas of any species of mammals. Thus, the 132 does not provide support for the full breadth of mammalian pancreatic tissue yielding the same types of differentiated cells.

With regard to the 132 of February 26, 2008 indicating that the cells obtained from goat glandular tissue can differentiate into the 3 germ layers, this does not provide support that the specification was enabling at the time of filing that any glandular tissue was a source of pluripotent stem cells. The issue at hand is that the art at the time of filing teaches than an artisan cannot predict whether any stem cell obtained from tissue is pluripotent and the art teaches than an artisan cannot predict what cells the pluripotent cells differentiate into following induction of the cells to differentiate (see Office Action, December 15, 2006, pages 6-7). The 132 of February 26, 2008 indicates that different types of differentiated cells (see 132, point 7) of the three germ layers were obtained from the goat salivary glands. The 132 also indicates that the differentiated cells stained positive for several cell markers having specificity for different cells of all 3 germ layers (132, filed February 26, 2008, point 7) and thus indicates that the differentiated cells of salivary gland are different from those of rat and human pancreas tissue. (It is noted at this time that the 132 refers to figures of cell stainings. However, no figures were provided with the 132.) The 132 declaration is

further support for the unpredictability in the art that an artisan cannot reasonably predict that stem cells from other tissues differentiate into the same cell types. It is undue experimentation for an artisan to predict that pluripotent stem cells have been obtained when an artisan cannot predict what kinds of differentiated cells will be obtained when the pluripotent cells are induced to differentiate. It is undue experimentation to determine what kind of differentiated cells are obtained following induction of differentiation because the art teaches that there are no set types of tissues that pluripotent stem cells differentiate into.

With regard to the issue of "nestin" wherein the marker is indicative for a neuronal stem cell, Applicant indicates that the marker is a general stem cell marker and refers to Weise et al., 2004 and Zulewski et al., 2001 (Applicant's response, page 6). Applicant indicates that Weise et al., 2004 has been submitted with the instant response, however, the Examiner cannot find the publication and cannot comment on Weise et al. With regard to Zulewski et al., Zulewski et al. was provided as part of Applicant's IDS, January 10, 2005. In response, Zulewski et al. indicate that cells that express nestin differentiate into pancreatic and hepatic cells. As such, nestin is not so limited to cells of the neural lineage. The rejection as it applies to this issue is withdrawn.

Thus, the claims remain rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10-13 remain rejected under 35 U.S.C. 102(b) as being anticipated by Schneider et al. 2001, Am J. Physiology, Cell Physiol., 281: C532-543, see IDS, previously cited, as evidenced by Kruse et al., 2004, Appl. Phys. A, 79: 1617-1624, see IDS previously cited for reasons of record, December 15, 2006 and July 24, 2007.

Claims 10-13 remain rejected are newly rejected under 35 U.S.C. 102(b) as being anticipated by Apte et al., 1998, Gut, 43: 128-133, see IDS, previously cited, as evidenced by Kruse et al., 2004, Appl. Phys. A, 79: 1617-1624, see IDS previously cited for reasons of record, December 15, 2006 and July 24, 2007.

Applicant's arguments filed January 24, 2008 have been fully considered and they are persuasive in part.

Applicant indicates that claim 3 has been amended to use the phrase, "consisting of" and that the phrase excludes differentiated cells from the compositions disclosed by Schneider et al. and Apte et al. In response, this is persuasive. The rejection of claims 3, 5-9 has been withdrawn. It is noted that the rejection of claims 1, 2, 4 have been withdrawn as the claims have been cancelled.

With regard to claim 14 being amended to a stem cell cultured obtained from exocrine glandular tissue that is obtained from salivary gland, lacrimal gland, and a sudoriferous gland and/or sebaceous gland, neither Schneider et al. nor Apte et al. teach that their cells were obtained from these glands. As such, the rejection as it applies to this claim is withdrawn.

Applicant indicates that claims 10-13 use the phrase, "consisting essentially of" and excludes the differentiated cells of Schneider et al. and Apte et al. In response, this is not persuasive. According to MPEP 2111.03, for purposes of searching and applying prior art under 35 USC 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." Because the specification does not indicate what parameters is meant by "consisting essentially of" of the claimed culture, claims 10-13 has been interpreted as "comprising" and the rejection of claims 10-13 remains.

Claims 3, 5-13, 59, 60 are newly rejected under 35 U.S.C. 102(e) as being anticipated by Roberts et al., US Patent 6,436,704, patented August 20, 2002.

Roberts et al. teach that human fetal pancreas was mechanically pulled apart and enzyme treated. The cell aggregates were then washed and spun by centrifugation and were plated in fibronectin-coated wells at 37 degrees Celsius in a humidified 5% carbon dioxide incubator for 72 hours. After 72 hours, the epithelial cells formed suspended spherical structures and the mesenchymal or stromal cells were attached to

the surface of the well. When a monolayer of the epithelial cells is desired, the pancreatic aggregates or pancreatic spheres were plated on a collagen-coated dish (Roberts, Example 1).

Claim 3 is drawn to a composition consisting of isolated pluripotent adult stem cells. It is interpreted that the cells taught in the instant specification consists of only pluripotent stem cells because differentiated acinar cells die in the culture condition of 37°C, humidity, and 5%CO_2. Roberts et al. teach the same method steps described in the specification of the instant Application. As such, the population of cells plated in the fibronectin-coated wells is the same as that claimed. While Roberts et al. describe a way of separating pancreatic progenitor cells from stromal cells by using fibronectin coating on the wells, the cells in the fibronectin-coated wells are the same as those of the instant specification as the cells of Roberts et al. were obtained the same way as that of the instant specification.

As such, Roberts et al. anticipate the claimed invention.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Joanne Hama/
Art Unit 1632